AMENDMENTS TO THE CLAIMS

This listing of the claims will replace all prior versions and listings of the claims:

1. (**Withdrawn**) A method of modulating a biological response in a cell, the method comprising contacting the cell with at least one agent that modulates the expression or activity of Errα or Gabp, wherein the biological response is

(a) expression of at least one OXPHOS gene;

(b) mitochondrial biogenesis;

(c) expression of Nuclear Respiratory Factor 1 (NRF-1);

(d) β-oxidation of fatty acids;

(e) total mitochondrial respiration;

(f) uncoupled respiration;

(g) mitochondrial DNA replication;

(h) expression of mitochondrial enzymes; or

(i) skeletal muscle fiber-type switching.

2-16. (**Canceled**)

17. (**Withdrawn**) A method of determining whether an agent is a potential agent for the treatment of a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function, the method comprising determining whether the agent increases:

(i) the expression or activity of Errα or Gabp in a cell; or

(ii) the formation of a complex between a PGC-1 polypeptide and (i) an Errα polypeptide; or (ii) a Gabp polypeptide;

wherein an agent that increases (i) or (ii) is a potential target for the treatment of the disorder.

18. (**Canceled**)

19. (**Withdrawn**) The method of claim 17, wherein the agent increases the formation of the complex, and wherein the agent increases the biological response.

20-34. (**Canceled**)

35. (**Withdrawn**) A method of reducing the metabolic rate of a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of an agent which decreases the expression or activity of at least one of the following:

(i) Errα;

(ii) Gabpa;

(iii) a gene having an Errα binding site, a Gabpa binding site, or both; or

(iv) a transcriptional activator which binds to an Errα binding site or to a Gabpa binding site;

thereby reducing the metabolic rate of the patient.

36-41. (**Canceled**)

42. **(Withdrawn)** A method of identifying a susceptibility locus for a disorder that is characterized by reduced mitochondrial function, glucose intolerance, or insulin intolerance in a subject, the method comprising

(i) identifying at least one polymorphism in a gene, or linked to a gene, wherein the gene (a) has an Errα binding site, a Gabpa binding site, or both; or (b) is Errα, Gabpa, or Gabpb;

(ii) determining whether at least one polymorphism is associated with the incidence of the disorder,

wherein if a polymorphism is associated with the incidence of the disorder then the gene having the polymorphism, or the gene to which the polymorphism is linked, is a susceptibility locus.

43-46. (**Canceled**)

47. **(Withdrawn)** A method of determining whether a subject is at risk of developing a disorder which is characterized by reduced mitochondrial function, the method comprising determining whether a gene from the subject contains a mutation which reduces the function of the gene, wherein the gene has an Errα binding site, a Gapba binding site, or both, wherein if a gene from the subject contains the mutation then the subject is at risk of developing the disorder.

48-77. (**Canceled**)

78. **(Withdrawn)** A method of detecting statistically-significant differences in the expression level of at least one biomarker belonging to a biomarker set, between the members of a first and of a second experimental group, comprising:

(a) obtaining a biomarker sample from members of the first and the second experimental groups;

(b) determining, for each biomarker sample, the expression levels of at least one biomarker belonging to the biomarker set and of at least one biomarker not belonging to the set;

(c) generating a rank order of each biomarker according to a difference metric of its expression level in the first experimental group compared to the second experimental group;

(d) calculating an experimental enrichment score for the biomarker set by applying a non-parametric statistic; and

(e) comparing the experimental enrichment score with a distribution of randomized enrichment scores to calculate the fraction of randomized enrichment scores greater than the experimental enrichment score, wherein a low fraction indicates a statistically-significant difference in the expression level of the biomarker set between the members of the first and of the second experimental group.

79-92. (**Canceled**)

93. (**Previously Presented**) A method of identifying an agent that regulates expression of OXPHOS-CR genes, the method comprising

(a) contacting (i) an agent to be assessed for its ability to regulate expression of OXPHOS-CR genes with (ii) a test cell; and

(b) determining whether the expression of at least two OXPHOS-CR gene products show a coordinate increase in the test cell compared to an appropriate control, wherein a coordinate increase in the expression of the OXPHOS-CR gene products indicates that the agent regulates the expression of OXPHOS-CR genes.

94-105. (**Canceled**)

106. (**Previously Presented**) The method of claim 93, wherein a coordinate increase in the expression of the OXPHOS-CR gene products further indicates that the agent is a potential enhancer of the expression or activity of Errα or Gabp.

107. (**Previously Presented**) The method of claim 106, wherein a coordinate increase in the expression of the OXPHOS-CR gene products further indicates that the agent is a potential agent for enhancing mitochondrial biogenesis, expression of Nuclear Respiratory Factor 1

(NRF-1), β-oxidation of fatty acids, total mitochondrial respiration, uncoupled respiration, mitochondrial DNA replication, expression of mitochondrial enzymes, or skeletal muscle fiber-type switching.

108. (**Previously Presented**) The method of claim 93, wherein the agent to be assessed is a small molecule.

109. (**Previously Presented**) The method of claim 93, wherein a coordinate increase in the expression of the OXPHOS-CR gene products indicates that the agent is a potential agent for the treatment of a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

110. (**Previously Presented**) The method of claim 93, wherein a coordinate increase in the expression of the OXPHOS-CR gene products further indicates that the agent is a potential agent for increasing expression or activity of Errα or Gabp.

111. (**Previously Presented**) The method of claim 110, wherein an agent that increases expression or activity of Errα or Gabp is a potential agent for the treatment of a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

112. (**Previously Presented**) The method of claim 110, wherein the test cell is a mammalian cell.

113. (**Withdrawn**) The method of claim 93, further comprising assessing the effect of the agent on mitochondrial number or on a mitochondrial function.

114. (**Withdrawn**) The method of claim 93, further comprising assessing whether the agent increases a desired biological response that is impaired in subjects having a disorder that is characterized by glucose intolerance, insulin resistance, or decreased mitochondrial function.

115. (**Currently Amended**) The method of claim 93, wherein step (a) comprises contacting (i) an agent to be assessed for its ability to regulate expression of OXPHOS-CR genes with (ii) a test cell ~~is performed~~ in vitro, and the method further comprises (c) administering the agent to a mammalian organism.

116. (**Previously Presented**) The method of claim 115, wherein the mammalian organism is human.

117. (**Previously Presented**) The method of claim 115, wherein the mammalian organism is a test animal that serves as a model for a disorder characterized by glucose intolerance, insulin resistance, or decreased mitochondrial function.

118. (**Previously Presented**) The method of claim 93, wherein the test cell is a mammalian cell.

119. (**Previously Presented**) The method of claim 118, wherein the test cell is a skeletal muscle cell.

120. (**Previously Presented**) The method of claim 118, wherein the test cell is in an organism.

121. (**Previously Presented**) The method of claim 118, wherein the agent to be assessed is a small molecule.

122. (**Previously Presented**) The method of claim 93, wherein the method is performed in parallel on multiple populations of cells and each population is contacted with a different agent to be assessed.

123. (**Previously Presented**) The method of claim 122, wherein the agents are members of a compound library.

124. (**Previously Presented**) The method of claim 109, wherein the agent is useful for treating a human suffering from a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

125. (**Previously Presented**) The method of claim 111, wherein the agent is useful for treating a human suffering from a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

126. (**Previously Presented**) The method of claim 93, further comprising determining whether the agent also regulates expression of genes that are not OXPHOS-CR genes.

127. (**New**) The method of claim 93, wherein step (a) comprises contacting (i) an agent to be assessed for its ability to regulate expression of OXPHOS-CR genes with (ii) a test cell in vitro.